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Food and Drug Administration  
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Room 1061  
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To whom it may concern

**DOCKET NUMBER 98P-0504**

Please find attached comments the New Zealand Ministry of Agriculture and Forestry (MAF) has at this time with respect to the establishment of a Performance standard for *Vibrio vulnificus*. MAF is the technical agency within New Zealand responsible for assuring the food safety of exports of shellfish.

If you require an explanation of any details contained in this submission or further information, please feel free to contact this office.

Yours sincerely

A handwritten signature in cursive script, appearing to read "Bill Jolly".

Dr WT Jolly  
Counsellor (Veterinary Services)

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## SECTION 1 INTRODUCTION

New Zealand has a significant shellfish industry and has a Memorandum of Understanding (MOU) with the United States FDA which allows us to export fresh and frozen shellfish to your country. The MOU requires us to abide by the provisions of the National Shellfish Sanitation programme and we are regularly audited by the USFDA for compliance with this standard.

To date New Zealand has had no cases of Vibrio vulnificus (Vv) associated with commercially harvested shellfish<sup>1</sup>. However, we acknowledge that this pathogen is a significant public health problem in the USA that is proving a challenge for public health policy makers. The decisions made by the USFDA on this matter, may have consequential affects for our shellfish industry or on how we manage similar public health problems in NZ. Therefore, the Ministry of Agriculture and Forestry (MAF) believe it important to take the opportunity to comment on the proposed Vv performance standard.

## SECTION 2 RISK ASSESSMENT AND MANAGEMENT TOOLS

The issues surrounding Vv are complex and potentially affect many stakeholders. In such situations MAF supports the use of the Risk Analysis model to assess how best to manage public health problems. The Risk Analysis model is endorsed worldwide by reputable organisations as the World Health Organisation and the US Environmental Protection Agency. Risk Analysis consists of two phases: Risk Assessment and Risk Management.

A suggested Risk Analysis Management framework<sup>2</sup> is as follows:

- 1) Define the problem and put it in context.
- 2) Analyze the risks associated with the problem in context.
- 3) Examine options for addressing the risks.
- 4) Make decisions about which option to implement.
- 5) Take actions to implement.
- 6) Conduct an evaluation of the results of the actions.

The framework should be conducted in collaboration with stakeholders. Iterations should be made as new information emerges.

It is acknowledged that to date each of these steps have been undertaken by the USFDA in conjunction with the ISSC. We summarise our understanding of the Vv issues using these steps.

## A: THE PROBLEM

Vibrio vulnificus is a naturally occurring organism, found in the marine environment in many places throughout the world. Therefore, consumption of raw seafood, particularly filter feeding shellfish, has the potential to cause adverse health effects. Gastroenteritis occasionally occurs in healthy individuals, but affects are much more serious in certain segments of the population. The “at-risk” population are immune compromised - in particular with alcoholic liver disease, diabetes, haemochromatosis, chronic Hepatitis B and C.

To date most cases in the USA have been associated with consumption of raw oysters harvested from the states bordering on the Gulf of Mexico.

There is still much unknown about the pathogen Vv eg cause of virulence, infection dose, which strains are pathogenic and survival rates outside the marine environment.

## B: ANALYZE THE RISKS

It is thought that there are 12-30 million of persons in the “at-risk” group in the USA. However, the incidence rate of the disease is low. Using data from the 1995 Behavioural Risk Factor Survey(BRFS)<sup>3</sup> for Florida state and disease notifications in that state suggests that the incidence of Vv in those with liver disease is 20 per 100,000 while the incidence in those without liver disease is 12 per 100,000. The incidence for those who did not eat raw oysters was very small indeed 0.104 per 100,000.

However, the health consequences for those affected are significant; septicaemia, shock and mortality in over 50% of the cases.

## C: DEFINE THE RISK MANAGEMENT OPTIONS

To date the options for Risk Management have included:

- i) Prohibition of harvest.
- ii) Education of consumers, including compulsory labelling.
- iii) Treatment of product post harvest.

## D: DECISIONS ABOUT OPTIONS AND IMPLEMENTATION ISSUES

Over the years it would seem that the Risk Management options for Vv have been carefully considered. Although much research has been undertaken and the USFDA has sponsored two multi-disciplinary workshops no reliable method has been found for

eliminating Vv in shellstock in the growing areas or by depuration. It is understood that only heat treatment ensures total elimination of the organism

To date the USFDA have used mainly used persuasion and recommendation techniques in their regulatory role.

Much health education has been undertaken, aimed at advising those in the "at-risk" groups of their potential susceptibility in eating raw shellfish. However, it is important to acknowledge that a portion of the population will not be aware that they are in the susceptible group ie they have not been medically diagnosed, have not been informed by the medical practitioner or have not understood their status.

It would also seem that raw shellfish oyster eaters may be Risk Takers - ie although they are aware of the potential risks associated with raw shellfish consumption they choose to take the risk exposure (gamble). This risk taking characteristic has been documented<sup>4</sup>. Data from the 1995 BFRS Florida state results also supports this theory. The group in which raw oyster consumption patterns had increased were males aged 18-44 years who earned more than US\$50,000 per annum. This group also showed good understanding of the risks (86.3% had heard of the risks).

In June 1993<sup>5</sup> it became compulsory for all food service establishments in Florida and several other states serving raw oysters to display either on menus, table placards or elsewhere in plain view of all patrons, the following notice:

"Consumer Information: There is risk associated with consuming raw oysters. If you have chronic illness of the liver, stomach or blood or have immune disorders, you are at greater risk of serious illness from raw oysters and should eat oysters fully cooked. If unsure of your risk, consult a physician"

It would appear that these warning notices have reduced raw oyster consumption patterns. When questioned during the 1995 BRFS of their cognizance of this warning, 55% of those who had eaten raw oysters in the last year had seen these warning notices and of these 33% (209,418) stated that it had influenced whether they had ordered or not.

The 1995 BRFS also found that the majority of persons ate their raw oysters at a restaurant, therefore it would seem that this is an appropriate venue for the warnings to be displayed.

In 1995 the Interstate Shellfish Sanitation Conference decided to mandate stricter time/temperature harvesting controls in those states where two or more cases caused by Vv had occurred and been epidemiologically implicated with oysters from their growing areas. This requirement was undertaken with full knowledge that the pathogenic dose was not known.

## D: EVALUATION OF THE RESULTS OF THE ACTIONS

Even with all actions listed above, the number of cases of Vv has not decreased in the USA each year. The reason for the continuing upward trend is still not known - it could be due to changing environmental or human behaviour patterns. Therefore, it is timely to consider what further steps can be taken.

Other options could include:

- i) Prohibition of harvest.
- ii) Post harvest treatment of shellfish.

We understand that there is now at least one food technology process available which could be applied to oysters and thus ensure that there are non-detectable levels of Vv. The USFDA have reviewed the data submitted by AmeriPure Co and it is considered that the process is capable of reducing Vv to non-detectable levels.

## SECTION 3: NEW ZEALAND'S OPINION ON THE PETITION

On assimilating the above information summarised in Section 2 , we would support the petition; non-detectable levels of Vv in raw molluscan shellfish harvested from waters that have been linked to illnesses or deaths

Our rationale for the support is due to the fact that the current Risk Management techniques employed by the USA for Vv have not reduced the number of human cases. Therefore, further appropriate public health measures should be taken to protect the consumer. Technology is now available to treat the shellfish which will ensure that virulent Vv is eliminated. Such treatment measures have been used successfully to manage other similar public health problems in the food chain around the world eg pasteurisation of milk products, addition of iodine to salt to reduce the incidence of goitre.

However, it is acknowledged that careful consideration needs to be given to the implementation of this management option. Strict guidelines will need to be written to define "epidemiological implication" and boundaries of growing waters so that harvesters are not unfairly penalised. Thought will need to be given on how to ensure compliance - how the shellfish should be treated and where control mechanisms should be placed to ensure non-complying shellfish does not reach the market

We would also support the continuation of the current Risk Management techniques used, namely:

- 1) Continued research to learn more about pathogen ie infective dose, pathogenic strains etc. This research would allow Risk Management techniques to be further rationalised.

2) Health education of the population of the risks. If all commercially harvested shellstock is treated, then this information will be appropriate for recreational gatherers.

## SECTION 4: ANSWERS TO SPECIFIC FDA QUESTIONS

We respond to the specific questions posed in your notice

1) AmeriPure technology readily employable? - in New Zealand we do not have access to the specific technical details of the process and therefore are unable to comment on barrier issues. However, from our limited knowledge of the process it seems that it could be implemented as a routine treatment step post harvest and prior to reaching the consumer.

2) Other technologies? - again we do not have specific details of technologies currently or imminently available in the USA. It is understood though that apart from the pasteurisation techniques, other developments are potentially available eg pressure processes. We would support technologies that were shown to reduce by the USFDA to routinely eliminate Vv and which can be practically and economically introduced into the food process chain.

3) Reliability of technologies - as stated in Point 2 above we would support implementation of technologies that the USFDA had confidence would eliminate Vv in those areas where oysters harvested had been epidemiologically implicated in two or more cases. If the process is mandated, there will be associated regulatory compliance costs.

4) Non-detectable level - with the current knowledge base for Vv, we could only support a non-detectable level as the acceptable limit for Vv. If further scientific knowledge gives adequate information on pathogenic dose levels and strains, the acceptable level could be reconsidered.

5) Performance standard for all molluscan shellfish? - at this stage the causative agent epidemiologically implicated is raw oysters from the Gulf of Mexico. Unless there is good evidence that other commercially harvested shellfish in a geographical area is a significant causal agent, the standard should only be applied to oysters.

6) Costs - obviously there are costs associated with the treatment process technology, however non-treatment will ensure continued medical costs associated with Vv cases. Although the oyster industry will initially pick up the costs of treatment, we are sure that these will be passed onto the consumer. Without knowing more about the specifics of the technology and industry costs in the USA we are unable to comment further.

Marine biotoxins have affected some shellfish growing areas in the United States and it is assumed that these areas are controlled differently than those areas not affected by the toxins. The economic issues in these areas may be similar to those affected by Vv.

Vv is a naturally occurring pathogen and therefore is different to many other pathogens associated with bivalve shellfish eg Salmonella. Since 1925 the USA has had some means of controlling the risks posed by bivalve shellfish and over the years this evolved into the National Shellfish Sanitation Programme. This programme has been adapted by many countries. The purpose of this programme is to prevent illness from shellfish by ensuring that harvest areas are not impacted by pathogens. Water monitoring for microbiological, chemical and marine biotoxin contamination is required, along with strict post harvest and processing controls. Faecal or Total Coliforms are used as the indicator organism for other pathogens. This programme has historically been very successful in preventing illness.

We do not believe that it would be cost effective or appropriate to replace this proven programme.

7) Benefits of a performance standard - hopefully the population will have a reduced incidence of Vv cases. It is acknowledged that those states who do not have to implement the treatment technology would have a possible market advantage.

8) Vibrio parahaemolyticus - at this stage we do not believe that the non-detectable standard should be implemented for other Vibrio species, including V parahaemolyticus (Vp). It is recommended that a sound Risk Assessment be undertaken before Risk Management techniques are implemented. It is understood that the USFDA are undertaking such an exercise for Vp. We would recommend that this exercise be successfully completed, before a non-detectable standard is considered for this pathogen.

However, if some growing areas are causing outbreaks of Vp, these areas should be closed for harvest until the Risk Assessment is completed.

## **SECTION 6: CONCLUSION**

MAF supports the petition request requiring non-detectable levels of Vibrio vulnificus in raw molluscan shellfish harvested from waters that have been linked to illnesses or deaths.

Care will need to be taken in implementing this requirement to ensure that it is fairly applied and appropriate compliance action is taken.

We should be pleased to provide further explanation of our submission or participate in future debate if you so require.

## **SECTION 7: REFERENCES**

- 1) McCoubrey D J: Risk of *Vibrio vulnificus* Infection Following Consumption of Raw Commercially Harvested North Island Oysters. MPH Thesis, University of Auckland 1996.
- 2) Presidential/Congressional Commission on Risk Assessment: Risk Assessment and Risk Management in Regulatory Decision Making. Final Report Vol 2 1997.
- 3) Personal Communication with Dr Hopkins, Chief Epidemiologist, Florida Department of Health.
- 4) Klontz KC, Desenclos JA, Wolfe LE, Hercherl SA, Roberts C; The Raw Oyster Consumer - A Risk Taker? Use of the Behavioural Risk Factor Surveillance System. *Epidemiology* Nov Vol2:437-439.
- 5) MMWR CDC June 1993: Vol 42: No 21



# **RISK ASSESSMENT OF VIBRIO VULNIFICUS INFECTION FROM NEW ZEALAND OYSTERS.**

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## **ABSTRACT**

Vibrio vulnificus (V. vulnificus) is a naturally occurring (autochthonous) pathogen and therefore cannot be controlled with the same methods that are suitable for sewage based problems eg Salmonella typhi.

The bacteria affects only a small "at-risk" group - those with liver problems and those with iron storage diseases, but the health consequences for those in the "at-risk group" are severe. Persons with pre-disposition exposed to V. vulnificus can suffer septicaemia with up to 70% mortality. Much is still not known about how or why V. vulnificus causes these severe health effects - the pathogenic dose and the infective strains are still to be identified.

V. vulnificus thrives in water above 17° Celsius and with salinity levels between 5-25ppt. Such parameters occur in estuaries and consequently raw oysters seems to be the common shellfish agent. Cooking quickly destroys the bacteria.

New Zealand undertook a study of the potential hazards associated with commercial shellfish operations causing V. vulnificus problems

This involved:

- i) an environmental risk assessment and a sampling programme in commercial oyster growing areas.
- ii) a survey of the stakeholders (bureaucrats, shellfish industry, at-risk persons, doctors and the general public) as to how they perceived the risks associated with V. vulnificus and how these risks should be managed.

The conclusions from the study were:

- i) The commercial oyster environment is not conducive to Vibrio vulnificus becoming endemic. The limiting factor is salinity.
- ii) There are statistically significant (>95%) different opinions amongst the various stakeholders. These opinion differences relate to risk perception and preferred risk management methods. 40% of the At-Risk group were prepared to expose themselves to the potential hazards of eating raw oysters.

**KEY WORDS:** Vibrio vulnificus, high mortality, environmental risk assessment, stakeholders perception

In 1976, a new pathogen was isolated and named Vibrio vulnificus, though many people have since called it the "monster of the deep". It is a salt-loving bacteria and was originally found along the coast of the United States, but since then has been isolated from a large number of marine sites around the world, including Asia, Holland, Australia and New Zealand. The organism thrives in estuarine waters with salinity and temperature parameters of between 5-25ppt and more than 17 degrees Celsius (Kaspar CW, Tamplin ML 1993).

The marine species Vibrio are naturally occurring and nutritionally play an important role in the food web, being fed on by other marine ciliates. In general V. vulnificus is found in association with the more benthic (bottom dwelling) species of plankton, arthropods, clams and oysters (dePaolo Proceedings of 1994 V. vulnificus Workshop).

If humans are exposed to the organism some may be affected by it and there have been a range of symptoms documented in numerous case histories in medical journals throughout the world. The symptoms have usually been noted to be:

- i) Primary septicaemia
- ii) Wound infections
- iii) Gastroenteritis

Primary septicaemia - results from the eating of uncooked seafood especially oysters. The mean incubation period is 16-38 hours. This condition is the most severe and occurs when V. vulnificus invades the bloodstream and disseminates throughout the body. The mortality rate is greater than 70% (Whitham, Proceedings of 1994 V. vulnificus workshop). It seems that the majority of these patients have some underlying chronic condition eg liver disease (especially cirrhosis and haemochromatosis) or some other disorder associated with immunosuppression, renal failure or diabetes (Johnstone, Becker and McFarland 1986).

Soft Tissue Wound Infections - with V. vulnificus commonly occur after shellfish injury or the exposure of pre-existing wounds to salt water. The wounds range from crab bites to penetrating injuries from preparing fresh shellfish. The infections typically being with swelling, redness, and intense pain around the site. Wound infections may be mild and self-limited or may progress to death (the mortality rate is up 22%). Infections can mimic gas gangrene in their rapidity and destructiveness and infections require immediate attention with antibiotics, surgical drainage, deep debridement and often amputation of digits or limbs.

Unfortunately much is still not known about the pathogenesis of V. vulnificus. To date the following has yet to be determined:

- i) the strains that are pathogenic (there are more than 70 strains and we do not yet know how to test for pathogenicity) (Hayat U, Reddy G P et al 1993).

ii) Cause of virulence.

iii) Infective dose

iv) Survival rates of the organism outside of the marine environment.

This lack of information makes it difficult for health professionals and regulators to decide how best to manage the pathogen. However, it is known that cooking very quickly and easily destroys the “monster” eg two minutes in a frypan at 180 degrees Celsius (Cook et al 1992).

## NEW ZEALAND SITUATION

In NZ there have been three documented cases of V. vulnificus. Two of these cases were wound infections and one a septicaemia case (Wright 1993).

Therefore, due to the issues surrounding the bacteria and potential health effects it was decided to undertake a health risk assessment of the situation in the NZ commercial oyster industry.

Risk assessment is worldwide becoming accepted as a suitable model to consider all the elements of a problem. It may also provide assistance with deciding on potential risk management techniques.

The subject of risk assessment is not a simple one and needs to be considered carefully depending on the risk one is considering and who is likely to be affected by this risk.

The accepted way of undertaking a Risk Assessment is by following four steps (USEPA 1993):

- 1) Hazard Identification - assess available information on hazards of organism.
- 2) Dose-response Assessment - determine the effect at different doses.
- 3) Exposure Assessment - estimate magnitude, duration and frequency of exposure.
- 4) Risk characterisation - combine the information from above to estimate the risk.

The World Health Organisation has established principles regarding environmental risk assessment and these include:

- 1) The public have the right to know actual or potential risks
- 2) Where there is uncertainty about risks to health this should be clearly stated.

3) Where there are issues contributing to poor health of particular groups these issues should be addressed specifically.

For the purposes of this Risk Assessment it was decided to use two approaches:

- 1) A Technical Analysis to ascertain whether the bacteria is likely to be in our commercially harvested oysters.
- 2) This was supplemented by an attempt to describe the perception of risk and options of risk management by a variety of groups.

## TECHNICAL ANALYSIS

### Hazard Identification

We have 14 commercial growing areas for Pacific oysters Crassostrea gigas in the North Island of New Zealand. All commercial area are required to implement a shellfish quality assurance programme which involves usually monthly water sampling using Faecal Coliforms as the indicator. During these water sampling runs water temperature and salinity measurements are taken.

The first step of our Hazard Identification was to peruse the records for the period 1991-1994 to ascertain whether the water temperature was above 17 degrees Celsius and or the salinity was between 5-25ppt.

### Exposure Assessment

Only four areas were found to have had historical environmental data that suggested that the organism would be present in the area. These areas were then sampled for four months (December, January, February and March 1995-96). These months are our summer months and this was considered to be the most likely period when the bacteria would be present.

12 oysters were taken to make each sample and they were then tested for V vulnificus using the USFDA culture methods and filters were taken for gene probe analysis.

On all sampling days the water was more than 17 degrees Celsius, but only three occasions did the salinity meet the optimum salinity measurement. However, all samples were negative for V vulnificus.

## RISK PERCEPTION QUESTIONNAIRE

With all these facts in mind it was decided to consult with the stake-holders on the possible health effects from V vulnificus. The stake-holders were deemed to be:

- \* the fishing industry
- \* health professionals
- \* the bureaucrats - Ministry of Health and the Ministry of Agriculture

- \* the at-risk (Diabetes Association and Kidney Transplant Group)
- \* the public

To undertake this consultation a leaflet describing the background facts on V. vulnificus was drafted along with a questionnaire asking whether the person would be prepared to expose themselves to the risk, whether the person considered themselves a risk-taker and how they thought the potential health problems should be managed.

There was a statistical difference in the answers from each of the groups.

Many of those in the at-risk group were prepared to expose themselves to the risk of eating raw oysters and when asked why responses included”

“At my age I have so many things wrong with me what does it matter if you enjoy so much.”

“They are the staple food on my birth place and Kai o Nga Rangatira Tipuna Matua.”

“Not enough evidence to stop me eating oysters which I love. I have ingested many thousand and I am still alive and kicking.”

“Because I enjoy them. If you stopped eating everything because of possibilities of infections, you wouldn’t eat at all”

If we consider the responses from the stakeholders administered the risk perception questionnaire then it is possible to see differences in that may related to possible types.

Thompson (1980) has suggested one prototype to apply to risk-takers.

Bureaucrats - this group relies on rules and procedures to cope with uncertainty. In the survey the bureaucrat wanted the most methods of protection implemented eg compulsory cessation of harvest, health warning labels and an education programme.

Entrepreneur - perceive risk taking as an opportunity to succeed in a competitive market and to pursue their personal goals. They are less concerned with equity issues and would like government to refrain from extensive regulation or risk management efforts. The survey data suggests the shellfish industry fit into this group - 55% were not concerned about this risk associated with eating oysters, 50% would eat raw oysters if they knew they were in the at-risk group, none wanted a compulsory label on the product.

Egalitarians - focus on long term effects of human activities and are more likely to abandon an activity than to take chances. They are concerned about equity. It would seem that the medical and general public fit into this category. Neither group would eat oysters if they were in the at-risk group. Both of these groups had more responses in the “Rarely” category when asked if they were likely to take risks.

Stratified - these people only trust themselves, likely to take a high risk for themselves but oppose any risk that they feel is imposed on them. Interestingly it would seem that the At-Risk group fits into this model. This group had the highest concern about those who may not know they were at-risk (65% very concerned) and yet 35% were prepared to take risks (higher than any other group). 40% were prepared to eat raw oysters even though they knew they suffered from disease that put them at-risk.

## CONCLUSIONS

1) The historical information analysis along with the survey to look for bacteria showed that currently environmental conditions in the North Island commercial oyster farms are not suitable for the survival of the organism. The salinity levels are too high for the bacteria to become endemic.

2) There are statistically significant (>95%) different opinions amongst the various stakeholders in NZ potentially involved in the issues surrounding this bacteria. These opinion differences relate to risk perception and preferred risk management methods. 40% of those in the At-risk group were prepared to expose themselves to the potential hazards of eating raw oysters.

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